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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/036,581	11/08/2001	Mina Alikani	PRO SE	4092

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EXAMINER	
BERTOGLIO, VALARIE E	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/036,581	ALIKANI ET AL.
	Examiner	Art Unit
	Valarie Bertoglio	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 November 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *06/24/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

11/08/2001

DETAILED ACTION

The response to the first office action and interview, filed 09/30/2003 has been entered. Claim 14 has been added. Claims 1-14 are pending and under consideration.

Specification

The objection to the abstract of the disclosure is maintained because applicant did not amend the abstract in reponse to the objection set forth on page 2 of the previous office action. Applicant requested that the Office make changes to the abstract. This can be done through an amendment by Applicant. Correction is required. See MPEP § 608.01(b).

Information Disclosure Statement

The information disclosure statement filed 11/08/2001 fails to comply with 37 CFR 1.98(a)(2). It has been placed in the application file, but the information referred to therein has not been considered.

Drawings

Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the U.S. Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

Applicant notes that black and white photographs will be submitted. This rejection will be withdrawn upon receipt of black and white drawings.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-8 and newly added claim 14 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Applicant's arguments filed 09/30/2003 have been fully considered but are not found persuasive for reasons elaborated below.

The composite blastocysts of claims 1-6, although comprised of cells from non-viable pre-embryos, are themselves viable, and appear to embrace human embryos. The stem cells of claims 7 and 8 can also be read to encompass human embryos. The claims, therefore, encompass viable, human embryos. Applicant argues that the composite blastocysts are not functional if implanted (page 1, paragraph 5). Applicant further argues that the non-viable composite human blastocyst is "intrinsically limited" and is "not expected" to be viable or give rise to a human being (page 2, lines 8-11). However, the specification fails to support that the claimed composite blastocyst is not capable of resulting in a live human. The intended use of the claimed composite blastocyst is a source of totipotent embryonic stem cells. Without evidence to the contrary, it is assumed that a composite blastocyst comprising totipotent embryonic stem cells that are capable

of generating a live birth is capable of forming a live organism, including human. Amendment of the claims to limit the composite blastocysts to those that are intrinsically limited or incapable of implantation may be sufficient to overcome the rejection. However, applicants are cautioned against adding new matter to the claims.

A human being is non-statutory subject matter. See 1077 O.G. 24, April 21, 1987.

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

Claim 14 is drawn to a preparation of composite blastocysts comprising cells derived from non-viable pre-embryos **obtained by nuclear transplantation.**

The specification provides no implicit or explicit support for the context of the breadth of obtained by nuclear transplantation encompassed by the bolded clause. The specification has only provided support for using cells derived from non-viable pre-embryos wherein the nucleus of the pre-embryo is derived directly from the nucleus of an egg and a sperm. Applicants are reminded that it is their burden to show where the specification supports any amendments to the

claims. See 37 CFR 1.121 (b)(2)(iii), the MPEP 714.02, 3rd paragraph, last sentence and also the MPEP 2163.07, last sentence.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. *Applicant should therefore specifically point out the support for any amendments made to the disclosure* [or point to case law supporting incorporation of such a limitation as in the instant case]" (emphasis added).

Written Description

Claims 1-13 and newly added claim 14 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's arguments filed 09/30/2003 have been fully considered but are not found persuasive for reasons elaborated below.

Claims 1-14 encompass a composite blastocyst from all species of animals including non-mammalian species. The specification describes composite blastocysts from mammalian species, specifically primate and humans (page 8, paragraph 4; page 10, paragraph 3). The specification discloses that composite blastocysts are formed by aggregating cells from non-viable pre-embryos in a protective environment of a zona pellucida. Only mammalian species comprise embryos within a zona pellucida and therefore the specification only describes aggregating mammalian cells from non-viable pre-embryos. The specification does not describe composite blastocysts from any non-mammalian species. Applicant argues that Byrne et al (April 2002, PNAS, Vol. 99, pp. 6059-6063) described the claimed aggregation process of the claimed invention. Description of the claimed invention by another, after the filing of the instant application, does not obviate the requirement for written description in the pending application. The teachings of Byrne fail to demonstrate that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-13 and newly added claim 14 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1,4-6,9 and 14 are unclear because they use the term pre-embryo. Applicant would like to define the term pre-embryo as pre-blastocyst and request addition of this definition to the specification. Changes to the specification can be made by applicant in an amendment to the specification, however, it is advised that Applicant be careful not to introduce new matter into the specification.

Claim 9 is incomplete as written. The preamble of the claim is directed to a method of producing composite blastocysts. However, the claim is incomplete because the steps of the method do not relate back to the preamble in a positive process. Appropriate correction is required. Claims 10-13 depend from claim 9 and are thus encompassed by this rejection.

Claim 11 is unclear because it recites the method of producing composite blastocysts of claim 9 wherein the cells used are derived from a viable embryo. However, the parent claim 9 does not encompass using cells from a viable embryo as it recites a limitation of non-viable pre-embryo (line 2). Therefore, claim 11 does not fall within the scope of parent claim 9. Appropriate correction is required.

Claims 12 and 13 are incomplete as written. They are drawn to a method of isolating stem cell lines but do not include method steps. Claims 12 and 13 include only the method of claim 9, which is drawn to producing composite blastocysts. Appropriate correction is required.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1) Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Luo (Nature, 1997, Vol. 388, pages 778-782) for reasons of record set forth on pages 7-8 of the previous office action and reiterated below.

Claims are directed to a preparation of composite blastocysts comprised of cells isolated from multiple, non-viable embryos. Claims recite that the CBs maintain the potential to differentiate (claim 2) into ectodermal, mesodermal and endodermal tissues (claim 3).

The term pre-embryo is not defined by the specification but is known in the art to include pre-implantation embryos (see above).

Luo teaches aggregating tetraploid mouse embryos, which are non-viable pre-embryos because they have not implanted in the uterus and cannot themselves develop into an embryo, with pre-implantation homozygous mutant embryos that are normally non-viable (page 778, column 2, lines 29-31), to generate rescued tetraploid aggregation chimeras which were then allowed to develop in foster female hosts to stage e12.5, which is beyond the blastocyst stage, at which time they were killed (page 782, column 1, last paragraph). The use of tetraploid cells rescued the ERR-beta mutant phenotype and the mutant chimeras appeared the same as wild-type (page 781, column 1, lines 20-21), This, composite embryos at E12.5 comprise tissue derivatives of all three germ layers. Hence, Luo generated composite blastocysts comprising cells derived from non-viable tetraploid and ERR-beta mutant embryos that had the potential to differentiate into derivatives of ectodermal, mesodermal and endodermal origin. Therefore, the teachings of Luo anticipate all the limitations of claims 1-3.

Applicant argues that Luo and Nagy (see below) do not include teachings of removing single nucleated cells from several non-viable embryos to form an aggregate. However, these limitations are not cited in the claims. Accordingly, the rejection is maintained.

2) Claims 1-3 and 7 remain rejected under 35 U.S.C. 102(b) as being anticipated by Nagy (PNAS, 1993, Vol. 90, pages 8424-8428) as set forth on page 8 of the previous office action and reiterated below.

Claims are directed to a preparation of composite blastocysts comprised of cells isolated from multiple, non-viable pre-embryos. Claims recite that the CBs maintain the potential to differentiate (claim 2) into ectodermal, mesodermal and endodermal tissues (claim 3). Claim 7 is directed a stem cell line.

The term pre-embryo is not defined by the specification but is known in the art to include pre-implantation embryos (see above).

Nagy taught aggregating tetraploid mouse embryos, which are non-viable pre-embryos because they have not implanted in the uterus and cannot themselves develop into an embryo, with ES cells, which are non-viable pre-embryos because they have the potential to develop into an embryo but cannot, in and of themselves, develop into a viable blastocyst (page 8424, column 2, last paragraph). The aggregation chimeras were then allowed to develop into live animals, which is beyond the blastocyst stage (page 8426, column 2, first full paragraph). Live animals possess tissue derivatives from all three germ layers and thus it is inherent that the cells at the blastocyst stage possessed the potential to differentiate into endoderm, mesoderm and ectoderm. Hence, Nagy generated composite blastocysts comprising cells derived from non-viable tetraploid embryos and ES cells. In addition, claim 7 is a product by process claim in which the

process of creating the animal carries little patentable weight. It is only the product, which is anticipated by the prior art and not the process by which the product was made. This is because the final product (a stem cell line) is not distinguished by any particular features or characteristics resulting from the process by which it is made. As such, the limitations of the claimed stem cell line are met by any stem cell line in the prior art. Patentability of a product-by-process claim is determined by the novelty and nonobviousness of the claimed product itself without consideration of the process for making it which is recited in the claims. *In re* Thorpe, 227 USPQ 964 (Fed. Cir. 1985).

Nagy taught mouse embryonic stem cells (page 8424, column 2, last paragraph), which are encompassed by the claimed stem cells of claim 7.

Thus, the teachings of Nagy anticipate the limitations of claims 1-3 and 7.

Applicant argues with respect to claims 1-3, that Luo (see above) and Nagy do not include teachings of removing single nucleated cells from several non-viable embryos to form an aggregate. However, these limitations are not cited in the claims. Accordingly, the rejection is maintained.

3) Claims 7 and 8 remain rejected under 35 U.S.C. 102(b) as being anticipated by Thomson (Science, 1998. Vol. 282, pages 1145-1147) as set forth on page 9 of the previous office action and reiterated below.

Claims are directed to a stem cell line produced by the process of claim 1 (claim 7) or claim 6 (claim 8). Claim 7 encompasses any stem cell line and claim 8 is limited to human stem cell lines.

Claims 7 and 8 are a product by process claims in which the process of creating the animal carries little patentable weight, as explained above.

Thomson taught generating human embryonic stem cell lines from human blastocysts (page 1145, column 2, lines 8-12 and page 1147, reference 6).

Therefore, Thomson meets all of the limitations of claims 7 and 8.

Applicant argues that the cells of Thomson are not derived from composite blastocysts from nonviable discarded human pre-embryos (page 3, 3rd paragraph). However, as stated above, the process by which the product is created carries little patentable weight. Without demonstrating that the cells of the invention are materially different from those of Thomson, the cells of the instant invention are anticipated by Thomson.

Applicant also argues that the source of the embryonic stem cells determines whether the research on the stem cells is funded by the NIH. Applicant further states the process by which the ES cells are isolated represents a paradigm shift in human embryology. These arguments, while their truth and importance cannot be negated, does not impact the patentability of the claimed products. Finally, applicant argues that "We claim 'composite-blastocyst-derived stem cells'". This language is not used in the claims. Furthermore, the specification fails to demonstrate that "composite-blastocyst-derived stem cells" differ in any way from the ES cells of Thomson.

Allowable Subject Matter

The following claim 9 is drafted by the examiner and considered to distinguish patentably over the art of record in this application, is presented to applicant for consideration:

9. A method of producing composite blastocysts comprising:

a) dissociating non-viable mammalian pre-blastocyst embryo into non-nucleated and individual nucleated cells or groups of cells;

b) isolation of individual mononucleated cells or groups of mononucleated cells from disaggregated non-viable pre-embryos;

c) aggregation of isolated mononucleated cells or groups of mononucleated cells from non-viable pre-embryos in a host zona pellucida, and

d) culturing of the zona-encapsulated cell aggregates to allow multiplication and differentiation of cells to form a composite blastocyst.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to

the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed. The Notice of Appeal must be accompanied by the required appeal fee of $330.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims or complies with a formal requirement made earlier. Amendments touching the merits of the application which otherwise might not be proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

A reply under 37 CFR 1.113 to a final rejection must include the appeal from, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is 703-305-5469. The examiner can normally be reached on Mon-Weds 6:00-2:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on 703-305-4051. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

PETER PARAS
PATENT EXAMINER

Valarie Bertoglio
Examiner
Art Unit 1632